



## CORRESPONDENCE

# Fatal acute liver failure after intravenous amiodarone administration



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Acute hepatotoxicity is a rare adverse effect of intravenous administration of amiodarone, but may be fatal if not recognized early and treated in a timely manner. Herein we report two cases of acute liver failure after intravenous administration of amiodarone. One patient with cerebral infarction was admitted to our emergency department. He received intravenous amiodarone for the acute heart failure with paroxysmal atrial fibrillation (PAF). The patient developed acute liver failure (ALF) and died of multiple organ failure (MOF). The other patient was admitted to our emergency department due to PAF. Intravenous amiodarone was administered and the PAF was converted to a normal sinus rhythm 6 hours later. The patient developed ALF and acute renal failure (ARF). He was successfully treated with blood purification in combination with other conservative therapy. Neither patient had a history of alcohol abuse or hepatitis virus infection. Furthermore, abdominal ultrasound examinations showed no significant findings in either patient.

Most published reports on acute hepatitis following amiodarone administration show a similar pattern of symptoms and laboratory results, including elevated alanine aminotransferase, aspartate aminotransferase, and total bilirubin, but severe renal impairment is rare. In general, liver injury is rapidly reversible after

discontinuation of amiodarone and the fatality rate is low. As shown in [Table 1](#), we have found five case reports of fatal hepatotoxicity caused by intravenous amiodarone, published between 1984 and 2010.<sup>1–4</sup> Intravenous amiodarone was used in all five cases to treat supraventricular tachyarrhythmia, which is not regarded as the best indication of amiodarone. ARF was the major cause of death in patients with intravenous amiodarone-induced ALF. Although there are no randomized trials to confirm its efficacy, early continuous renal replacement therapy has become a major part of the management of patients with ARF and ALF.

The mechanism for intravenous amiodarone-induced hepatotoxicity is not fully understood. Polysorbate 80, an excipient used to maintain the stability of amiodarone in solution, is believed to be responsible for the hepatotoxicity. However, a recent case–control study argues that hepatotoxicity induced by intravenous amiodarone cannot be clearly differentiated from ischemic hepatitis, claiming that they are in fact the same entity.<sup>5</sup> Future studies should focus on the underlying mechanisms for intravenous amiodarone-induced ALF and ARF.

In summary, hepatotoxicity is a rare, but potentially fatal, adverse effect of intravenous amiodarone. Amiodarone indication should be followed precisely and hepatic and renal parameters should be carefully monitored during and after its administration. Early continuous hemofiltration may improve the prognosis of severe cases of acute renal and liver failures after amiodarone administration.

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**Table 1** Summary of five published cases of fatal hepatotoxicity after intravenous amiodarone administration.

Age/sex	Amiodarone dose until hepatotoxic signs (mg)	Indication	Laboratory parameters and symptoms of liver toxicity	Cause of death	Day of death from ALF	Histology	Ref
28, M	1500	Persistent Af	AST 20,040 U/L, ALT 20,360 U/L, bilirubin 116 $\mu$ mol/L, hyperammonemia, PT $\uparrow$ , hepatomegaly, anuria, requiring dialysis, encephalopathy	Hepatic coma and acute renal failure	14	n/d	1
60, M	1500	Persistent Af	ALT 570 U/L, AST 1200 U/L, bilirubin 95 $\mu$ mol/L, Cr 274 $\mu$ mol/L, PT $\uparrow$ , hepatomegaly, oliguria, hyperammonemia, renal failure, encephalopathy	Hepatic coma and acute renal failure	4	Confluent liver cell necrosis	1
75, F	600	Supra-ventricular tachycardia	ALT 60–70-fold $\uparrow$ , bilirubin 408 $\mu$ mol/L, jaundice, PT $\uparrow$ , encephalopathy,	Encephalopathy	31	n/d	2
64, M	1200	Af	ALT 9,308 U/L Bilirubin 64 $\mu$ mo/L Cr 332 $\mu$ mo/L. jaundice, PT $\uparrow$ , metabolic acidosis, acute renal failure	Metabolic acidosis acute renal failure	3	Extensive necrosis for drug or ischemia	3
59, M	1200	Af	AST 7,388 IU/L, ALT 5,352 IU/L, PT $\uparrow$ , Cr 328 $\mu$ mol/L requiring dialysis	Acute renal failure	3	Acute hepatic necrosis	4

Af = atrial fibrillation; ALT = alanine aminotransferase; AST = aspartate aminotransferase; Cr = creatinine; F = female; M = male; n/d = not determined; PT = prothrombin time.

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